

to 5000 rads. Although the natural history of anal intraepithelial neoplasia is not yet clearly defined, it is possible that adequate treatment and follow-up in his case may have prevented the malignant transformation.

This case emphasises firstly, the need to ensure adequate treatment and follow-up in such cases to prevent this complication and secondly, to perform biopsies in those who have recalcitrant or atypical warts.

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Photodynamic therapy for condylomata acuminata with local application of 5-aminolevulinic acid

In spite of the large therapeutic arsenal for the treatment of genital warts, results are still disappointing and relapse is common.

We performed a pilot study in which we investigated photodynamic therapy (PDT) with local application of 5-aminolevulinic acid (5-ALA). PDT is an experimental treatment modality for cancer in which tumour cells are killed as a result of photoactivation of a tumour-localising agent. 5-ALA is a precursor of protoporphyrin IX (PpIX) in the biosynthetic pathway of haem. Topically applied on some types of skin tumours it induces a temporarily increased PpIX level, without causing systemic photosensitisation. PDT with local application of 5-ALA has been used successfully by Kennedy *et al*¹ for superficial non-

melanoma skin cancer and actinic keratosis.

We report the preliminary results of an open prospective pilot of seven patients with genital warts. The aim of this study was to determine the efficacy and adverse effects of PDT with local application of 5-ALA for the treatment of condylomata acuminata (CA). The treated group consisted of four males and three females aged 18 years and older with CA, localised perianal, penile, perivulvar and intravaginal. Diagnosis was made on clinical appearance. No therapy had been given for at least six weeks. The patients did not use other medication except for oral contraceptives, did not suffer from other diseases and were not pregnant or lactating. During the treatment period use of sunbeds was prohibited. Patients were informed of the investigational nature of PDT and other options were explained and offered. An informed consent form was signed. The protocol had been approved by the medical ethics committee of our hospital. Photographic documentation was done before application of 20% w/w 5-ALA in instillagel (gel containing lidocaine hydrochloride, chlorhexidine digluconate, methylhydroxybenzoate and propylhydroxybenzoate). The area was covered with a gauze, soaked in this gel, subsequently occluded under plastic and well fixed with tape. After 14 hours this was removed and an anaesthetic cream (with lidocaine and prilocaine) was applied. Two hours later the site was exposed to argon dye laserlight, wavelength 630 nm up to a total dose of 100 J/cm². Light intensity was either 150 or 75 mW/cm². After exposure patients received paracetamol 6 times daily 500 mg and naproxen twice daily 500 mg for one day. During illumination in vivo fluorescence was measured by means of a video camera with a filter for 690 nm. Photographic documentation was performed after 1, 2, 4, and 12 weeks. Efficacy was measured using the percentage of eradicated warts. The results are shown in the table.

Three of the patients (nos 2, 3, and 4) had a long history of conventional treatment. Patient 4 got a very serious swelling of the penis the days following PDT. At present a teleangiectatic spot in the treatment area persists. The great drawback in this therapy is the pain during illumination. Patient 2 broke off treatment after she received half the light dose because of the pain and insisted on conventional therapy at once, so PDT effects could not be evaluated. Also patient 7 who suffered from vaginal condylomata acuminata broke off therapy after 15 seconds because of the intense pain. She was willing to wait and see for the results. Within two weeks the condylomata acuminata were necrotic.

These results, though in a very experimental stage, are promising. Pain is a major drawback. Up to now we did not use intralesional anaesthetics because of possible interference with PDT. A practical disadvantage is the relative long time that the 5-ALA has to be applied. Shorter application times will be investigated in the future.

The 5-ALA was kindly provided by Janssen Clinica, Geel, Belgium.

Results

Patient	Gender	Localisation of CA	Applied light dose (J/cm ²)	Percentage reduction	Follow up period
1	Male	Perianal	100	100%	> 3 months
2	Female	Perivulvar	50	Unknown	
3	Male	Perianal	100	75%	> 3 months
4	Male	Penile	100	100%	> 3 months
5	Male	Penile	100	Recurrence after 4 weeks	
6	Female	Perianal	100	100%	> 3 months
7	Female	Vulvovaginal	< 10	100%	4 weeks

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Systemically administered interferon alfa-2a prevents recurrence of condylomata acuminata following CO₂-laser ablation. The influence of the cyclic low-dose therapy regimen. Results of a multicentre double-blind placebo-controlled clinical trial

From placebo-controlled clinical trials it has been concluded that subcutaneous interferon (IFN) alfa-2a is not effective as a monotherapy in the treatment of refractory condylomata acuminata at a dose of 1.5 megaunits if given continuously three times a week for four weeks.¹ Contrasting results, however, have been obtained with IFN gamma given as a monotherapy "cyclically" up to 2 megaunits daily for 7 days, followed by a 4 week pause (1 cycle) for up to 4 cycles.² This has led to the hypothesis that either the type of IFN or the treatment regimen were responsible for the differences. In addition, another controlled study administering IFN alfa-2a (3 megaunits/tiw, s.c.) given continuously adjuvantly to CO₂-laser did not show any superiority to placebo,³ whereas a cyclic application of IFN alpha in an open study showed lower recurrence rates in the IFN group.⁴ Therefore, we argued that the therapy regimen used could be the main reason for the observed treatment failure.

In contrast, in our study IFN alfa-2a was given cyclically adjuvant to CO₂-laser, comprising 5 days treatment with 1 megaunit/day and a 4 week treatment-free interval (1 cycle) up to a maximum of 3 cycles, leading to a total of 15 megaunits of IFN alfa-2a. The follow-up lasted 18 weeks. The evaluation of efficacy was done by the comparison of recurrence rates at week 33. A total of 84 patients (equally distributed to the therapeutic arms) were included in the study, out of which 32 (IFN alfa-2a) and 35 (placebo) respectively were evaluated at week 33. At the endpoint of the

study 13 out of 32 (41%, 95% confidence interval, 24-59%) of the IFN group and 22 out of 35 patients (63%, 95% confidence interval 45-79%) of the placebo group showed a recurrence of the condylomata. This difference is significant at a level of significance of 5% ($\chi^2 = 3.312$, critical value for one-sided testing at 5% level: 2.076). Figure 1 shows the cumulative frequency of recurrence of the condylomata in relation to time after surgery. The log rank two-sided test revealed statistically significant differences at a 5% level ($p = 0.0174$). The treatment was generally well tolerated. Eight patients from each group (19%) complained of side effects, usually mild to moderate. No drop outs due to side effects were observed.

Summarising our data, it seems that cyclic application of low dose IFN alfa-2a adjuvant to CO₂-laser ablation is superior in the treatment of condylomata acuminata compared to adjuvant continuous application of interferon or placebo, both in terms of recurrence rate and time to recurrence.

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Herpes simplex virus infection in women: viral subtypes and epidemiological features in a district hospital

The incidence of genital herpes is reportedly on the increase in many parts of the UK,¹⁻⁴ and herpes simplex virus type 1 (HSV 1) has become the predominant subtype in genital infections in women.²⁻⁵ Reasons for the apparent increase in genital herpes in general, and HSV 1 in particular, are as yet unclear.

The aim of this study was to describe the proportions of HSV types 1 and 2 in women presenting with a first symptomatic episode of genital herpes at our genitourinary medicine (GUM) clinic; and compare clinico-epidemiological features of the two subtypes of HSV.

All women ($n = 121$) with a first sympto-

Cumulative frequency of recurrences of condylomata acuminata after treatment with interferon alfa-2a (Roferon®-A) and CO₂-laser in relation to time to recurrence.

